Incidence of Type 1 and Type 2 Diabetes in Adults Aged 30–49 Years

The population-based registry in the province of Turin, Italy

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OBJECTIVE — Incidence of type 1 diabetes is considered to be low in adults, but no study has been performed in Mediterranean countries.

RESEARCH DESIGN AND METHODS — We extended the study base of the registry of the province of Turin, Italy, to subjects aged 30–49 years in the period 1999–2001 to estimate the incidences of type 1 and type 2 diabetes. Diagnosis of type 1 diabetes was based on permanent insulin treatment or a fasting C-peptide level ≤0.20 nmol/l or islet cell (ICA) or GAD (GADA) antibody positivities.

RESULTS — We identified 1,135 case subjects with high completeness of ascertainment (99%), giving an incidence rate of 58.0 per 100,000 person-years (95% CI 54.7–61.5). The incidence of type 1 diabetes was 7.3 per 100,000 person-years (6.2–8.6), comparable with the rates in subjects aged 0–14 and 15–29 years (10.3 [9.5–11.2] and 6.8 [6.3–7.4]). Male subjects had a higher risk than female subjects for both type 1 (rate ratio [RR] 1.70 [95% CI 1.21–2.38]) and type 2 (2.10 [1.84–2.40]) diabetes. ICA and/or GADA positivities were found in 16% of the cohort. In logistic regression, variables independently associated with autoimmune diabetes were age 30–39 years (odds ratio [OR] 2.39 [95% CI 1.40–4.07]), fasting C-peptide <0.60 nmol/l (3.09 [1.74–5.5]), and BMI <26 kg/m^2 (2.17 [1.22–3.85]).

CONCLUSIONS — Risk of type 1 diabetes between age 30 and 49 years is similar to that found in the same area between age 15 and 29 years. Further studies are required to allow geographical comparisons of risks of both childhood and adulthood autoimmune diabetes, the latter being probably higher than previously believed.

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Epidemiological studies (1–7) have provided evidence that type 1 diabetes in adults is more common than previously believed. It has been estimated that almost 40% of people with type 1 diabetes develop the condition after 30 years of age (2). Classification based on clinical presentation can, however, underestimate the true number of cases arising among adults, many being misclassified as type 2 diabetes (8). The presence of markers of β-cell autoimmunity, such as islet cell (ICAs) and GAD (GADAs) antibodies, allows the identification of type 1 diabetes, independently of age and clinical presentation at disease onset (9). These markers are particularly useful in adults presenting a slowly progressive form of autoimmune disease known as latent autoimmune diabetes in adults (8). The relative proportions of type 1 and type 2 diabetes in adults depend on the reference population, probably being low in areas where the prevalence of obesity is high, as in the U.S. (10), and higher in areas with lower prevalences of overweight. In Italy, we previously showed that as much as 50% of incident cases in people with normal weight aged 30–54 years have at least one marker of β-cell autoimmunity and can be defined as type 1 diabetes (11).

As few population-based studies (1–7) have been conducted with individuals aged ≥30 years, the incidence of type 1 diabetes in adults is unknown in most areas. In northern Italy, the incidence rates among individuals ≤29 years of age have been estimated by the Registry of the Province of Turin, which has achieved high estimated completeness of ascertainment for both children and young adults (12–13). In this report, we aimed to extend the study base of the registry to people aged 30–49 years in the period 1999–2001 and to estimate the incidence rates of type 1 and type 2 diabetes by using both clinical and immunological features of incident cases.

RESEARCH DESIGN AND METHODS

— The study base was the resident population of the province of Turin, Italy, aged 30–49 years in the period 1 January 1999 to 31 December 2001 (2,165,000 inhabitants, 651,970 aged 30–49 years). All incident cases of diabetes (excluding gestational and secondary diabetes) arising during the study period were identified through diabetes clinics, to which patients are referred after diagnosis (primary source), and the centralized file of all patients who have obtained exemption from payment for drugs, syringes, and glucose-monitoring strips owing to a diagnosis of diabetes (secondary source) (12–13). All Italian citizens, irrespective of social class or employment, are cared for by a general practitioner as part of the National Health System. Primary care for diabetic patients

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Abbreviations: GADA, GAD antibody; ICA, islet cell antibody.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

is mainly provided by specialized diabetes clinics. All diabetic patients can obtain drugs and diabetes devices free of charge from the National Health System, provided they have certification of diabetes diagnosed by diabetologists working in public health clinics. Because of this procedure, almost all newly diagnosed patients attend one diabetes clinic at the onset of the disease.

Diabetologists were periodically contacted by the coordinating center to identify incident cases and to perform centralized measurements of markers of β-cell autoimmunity and fasting plasma C-peptide values within 1 year of diagnosis. In 2003–2004, the clinical charts of all diabetes clinics in the catchment area were reviewed to identify incident cases that had not been notified to the coordinating center and to assess the clinical features of individuals who had not been tested. Information on individuals identified only through the secondary source was obtained by collaboration with diabetologists and general practitioners.

A diagnosis of type 1 diabetes was based on permanent insulin treatment within 6 months of diagnosis, fasting C-peptide levels ≤0.20 nmol/l (14), or positivity for ICA or GADA. β-Cell function was estimated by centralized fasting plasma C-peptide measurement (normal values, 0.36–1.17 nmol/l; DPC, Los Angeles, CA). GADA was measured by a radioligand assay with human recombinant antigens (Medipan Diagnostica, Selchow, Germany); immunocomplexes were precipitated with protein A according to the method of Schmidli (15). GADA values >0.9 units/ml were considered to be positive. The sensitivity and specificity were 84 and 93%, respectively, at the first proficiency evaluation of the Diabetes Antibody Standardization Program (Lab ID 124) (16). ICAs were assayed by indirect immunofluorescence on frozen sections of human blood group 0 pancreas with fluorescein isothiocyanate–conjugated rabbit antibodies. ICA positivity was expressed in Juvenile Diabetes Foundation units (JDF-u) on a standard curve based on the international JDF-u reference sera sample. An ICA ≥5 JDF-u was considered positive. The sensitivity and specificity were 100% at the third ICA proficiency program of the Research Institute for Children, New Orleans, Louisiana (Lab ID 13).

The denominators of the incidence rates were intercensual estimates of the population of the province of Turin, Italy. The two-sample capture-recapture method was used to estimate completeness of ascertainment (17). The incidence rates in the age-group 0–29 years cover the period 1984–2001, and the rates in the age-group 30–49 years cover 1999–2001 to reduce the effect of annual instability of rates in children. The C-peptide values were nonnormally distributed and analyzed after logarithmic transformation. Differences in the clinical characteristics of incident cases were assessed by the test of variance for continuous variables and the χ^2 test for ordinal variables; the results are shown as means ± SD and geometric mean for normally and nonnormally distributed variables, respectively. Logistic regression analysis was then performed to assess the independent association between autoimmune diabetes (ICA or GADA positivity, dependent variable) and age (5-year age-groups), sex, BMI (<26, 26–29, >29 kg/m^2), and fasting C-peptide (quartiles). Since the odds ratios [ORs] were similar for the upper categories of age, C-peptide, and BMI, the reference in the final analyses was the lowest category, with aggregation of the upper ones, apart from age, which was categorized as 30–39 and 40–49 years. Logistic regression analysis was also performed using type of diabetes (type 2 = 0; type 1 = 1) as the dependent variable. The effect on estimated ORs of lag time between diagnosis and assessment of autoimmunity was assessed. The likelihood ratio test was used to test the significance of variables. All analyses were performed with Stata (Stata Release 8.0, Stata, College Station, TX). *P* values <0.05 were considered statistically significant.

RESULTS — In the period 1999–2001, 1,135 incident cases of diabetes in subjects aged 30–49 years were identified in the province of Turin: 1,026 through the primary source, 1,079 through the secondary source, and 970 through both, giving an estimated number of 1,141 subjects and a completeness of ascertainment of 99%.

The incidence rate of diabetes in the age-group 30–49 was 58.0 per 100,000 person-years (95% CI 54.7–61.5), with a significant increasing trend by age at onset (rate ratio [RR] 1.71[95% CI 1.62–1.80] for each age-group); the risk was 5.5-fold higher in the age-group 45–49 years than in the age-group 30–34 years (95% CI 4.47–6.79) (Table 1). Sex differences were found in all age-groups, male subjects having twofold higher risks than female subjects: the overall incidence rates per 100,000 person-years were 77.9 (95% CI 72.6–83.6) for male and 38.1 (34.5–42.2) for female (RR 2.04 [95% CI 1.81–2.31], $P < 0.0001$) (Table 1) subjects. The frequencies of overweight (BMI 26–29 kg/m^2) and obesity (BMI >29 kg/m^2) at onset of diabetes were 32.4 and 35.4% in male and 17.6 and 52.2% in female subjects, respectively ($P < 0.0001$). The frequencies of BMI >26 kg/m^2 increased markedly from the age-group 30–34 years to the age-group 45–49 years, particularly in female subjects: from 56.7 to 77.4% in male and from 43.3 to 81.6% in female subjects.

Markers of β-cell autoimmunity were assessed in 617 of 1,135 (54.4%) incident cases, with a median lag between diagnosis and assessment of 1.05 years (5th and 95th percentiles, 0.27–1.89 years). The causes of nonassessment were no notification of clinical appointments ($n = 471$), no informed consent ($n = 32$), and inadequate quantity of blood sample ($n = 15$). The tested subjects were younger (aged 42.4 years [interquartile range 38.8–46.9] vs. 43.9 years [41.3–47.5], $P < 0.0001$) and had lower BMI values (27.7 kg/m^2 [24.5–32.3] vs. 30.0 kg/m^2 [27.0–34.6], $P < 0.0001$) than untested subjects. Frequencies of treatment with diet, oral hypoglycemic drugs, and insulin at diabetes onset were 29.5, 49.6, and 22.9% in tested subjects and 29.1, 58.9, and 7.7% in untested subjects ($P < 0.001$). Treatment had not changed substantially over time; only 40 of the untested subjects were taking insulin since the onset of diabetes, and 17 of them had ketonuria. All of them had a clinical diagnosis of type 1 diabetes, no contraindication to oral drugs, and no alternative explanation for their permanent need of insulin treatment. Four tested and two untested subjects had had ketoacidotic coma at clinical onset, and all were receiving insulin.

As shown in Table 2, the proportion of tested subjects who were ICA or GADA positive was low (15.9%). Of 98 subjects with evidence of β-cell autoimmunity, only 15 were ICA positive. They were of similar age, BMI, and fasting C-peptide values with respect to those who were both ICA and GADA positive. Five subjects showing marker negativity had fasting C-peptide values ≤0.20 nmol/l were receiving insulin and were defined as having type 1 diabetes, as were 98 subjects with marker positivity and 40 insulin-treated untested subjects, giving a total of 143 with type 1 diabetes of 1,135 incident

Table 1—*Age- and sex-specific incidence rates of diabetes per 100,000 person-years in the province of Turin, Italy, 1999–2001*

	Male subjects		Female subjects		
Age-group (years)	Cases	Rates (per 100,000)	Cases	Rates per 100,000	Total
All diabetes					
30–34	69	26.2 (20.7–33.1)	38	14.8 (10.7–20.3)	107; 20.6 (17.0–24.8)
35–39	125	47.7 (40.0–56.8)	61	23.5 (18.3–30.2)	186; 35.7 (30.9–41.2)
40–44	237	101.7 (89.6–115.5)	100	42.5 (35.0–51.7)	337; 72.0 (64.7–80.1)
45–49	331	150.9 (135.5–168.1)	174	76.8 (66.2–89.1)	505; 113.3 (103.8–123.6)
All ages	762	77.9 (72.6–83.6)	373	38.1 (34.5–42.2)	1,135; 58.0 (54.8–61.5)
Type 1 diabetes					
30–34	20	7.6 (4.9–11.8)	12	4.7 (2.6–8.2)	32; 6.1 (4.3–8.7)
35–39	21	8.0 (5.2–12.3)	14	5.4 (3.2–9.1)	35; 6.7 (4.8–9.3)
40–44	22	9.4 (6.2–14.3)	15	6.4 (3.8–10.6)	37; 7.9 (5.7–10.9)
45–49	27	12.3 (8.4–17.9)	12	5.3 (3.0–9.3)	39; 8.7 (6.4–12.0)
All ages	90	9.2 (7.5–11.3)	53	5.4 (4.1–7.1)	143; 7.3 (6.2–8.6)
Type 2 diabetes					
30–34	49	18.6 (14.0–24.6)	29	10.1 (6.9–14.8)	75; 14.4 (11.5–18.1)
35–39	104	39.7 (32.7–48.1)	47	18.1 (13.6–24.1)	151; 29.0 (24.7–34.0)
40–44	215	92.3 (80.7–105.5)	85	36.2 (29.2–44.7)	300; 64.1 (57.2–71.8)
45–49	304	138.6 (123.9–155.1)	162	71.5 (61.3–83.4)	466; 104.5 (95.5–114.5)
All ages	672	68.7 (63.7–74.1)	320	32.7 (29.3–36.5)	992; 50.7 (47.7–54.0)

Data are *n*; incidence rates (95% CI).

cases. A clinical diagnosis of type 1 diabetes was performed by diabetologists in 92 of 143 (64.3%) incident cases. In contrast, all 992 subjects with type 2 diabetes were correctly defined using clinical criteria only. Incidence rates per 100,000 person-years in the age-group 30–49 years were 4.7 (95% CI 3.83–5.77) for clinical type 1 diabetes and 53 (50.2–56.7) for clinical type 2 diabetes.

The incidence rates of type 1 and type 2 diabetes are presented in Table 1. Sex differences were found in the risks for both diseases, male subjects having higher risks than female subjects for both type 1 (RR 1.70 [95% CI 1.21–2.38]) and type 2 (2.10 [1.84–2.40]) diabetes. Decreasing ratios of type 1 diabetes to all new cases of diabetes with increasing age were found in both sexes: 30% in the age-group 30–34 years, 19% in the age-group 35–39 years, 11% in the age-group 40–44 years, and 8% in the age-group 45–49 years. Incidence rates in subjects aged 30–49 years in the years 1999, 2000, and 2001 were 8.5 (95% CI 6.6–11.1), 5.4 (3.9–7.4), and 7.7 (5.8–10.1) for type 1 diabetes and 50.7 (45.5–56.5), 41.1 (36.6–46.3), and 58.0 (52.4–64.1) for type 2 diabetes, respectively.

Table 2—*Clinical and metabolic features of the population-based cohort of incident cases of diabetes in the province of Turin, Italy, aged 30–49 years in the period 1999–2001, at onset of diabetes by markers of β-cell autoimmunity*

	ICA and GADA positive	ICA negative GADA positive	ICA positive GADA negative	ICA and GADA negative	*P*
n	36 (5.8)	47 (7.6)	15 (2.4)	519 (84.2)	0.06
Male subjects (*n*)	17 (47.2)	29 (61.7)	10 (66.7)	355 (68.4)	0.06
Age (years)	40.2 ± 5.1	39.7 ± 5.5	44.1 ± 6.2	42.8 ± 5.1	<0.0001
BMI (kg/m^2)	24.2 ± 4.0	25.0 ± 6.8	27.5 ± 6.5	29.3 ± 6.0	<0.0001
BMI (%)					<0.0001
<26 kg/m^2	70.6	68.1	46.1	32.2	
26–29 kg/m^2	17.6	10.6	30.8	29.1	
>29 kg/m^2	11.8	21.3	23.1	38.7	
Plasma glucose (mmol/l)	17.0 ± 6.5	16.4 ± 5.3	13.8 ± 6.8	14.2 ± 6.4	0.02
Ketonuria (%)*	50.0	72.0	37.5	20.0	<0.0001
Poliuria (%)†	92	78.8	57.1	65.0	0.02
Weight loss (%)‡	82.6	69.7	42.9	46.7	0.001
Fasting C-peptide (nmol/l)	0.34 (0.23–0.59)	0.49 (0.32–0.76)	0.87 (0.66–1.54)	0.86 (0.66–1.19)	<0.0001
Insulin treatment	24 (66.7)	29 (63.0)	2 (13.3)	86 (16.9)	<0.0001
Insulin dependence (fasting C-peptide ≤0.20 nmol/l)	6 (16.7)	6 (12.8)	1 (6.7)	5 (1.0)	<0.0001

Data are means ± SD, *n* (interquartile range), or *n* (%), unless otherwise indicated. *Data missing for 345 subjects. †Data missing for 292 subjects. ‡Data missing for 314 subjects.

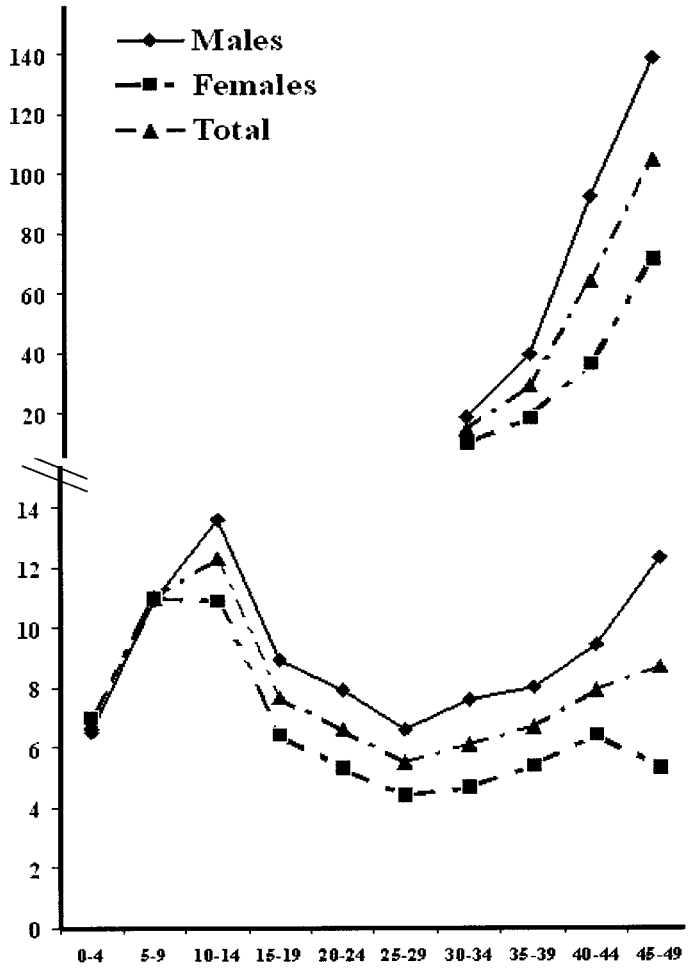

Figure 1—*Incidence rates per 100,000 person-years of type 1 and type 2 diabetes in the registry of the province of Turin. Subjects aged 0–29 years in the period 1984–2001; subjects aged 30–49 years in the period 1999–2001.*

Figure 1 shows the incidence rates in the registry of the province of Turin, by age at onset, in subjects aged 0–29 years in the period 1984–2001 (n = 1,133) and in subjects aged 30–49 years in the period 1999–2001 (n = 143). The incidence rates per 100,000 person-years of type 1 diabetes in the age-groups 0–14, 15–29, and 30–49 years were 11.0 (95% CI 9.9–12.3), 7.9 (7.1–8.8), and 9.2 (7.5–11.3) in male subjects; 9.6 (8.5–10.8), 5.6 (5.0–6.4), and 5.4 (4.1–7.1) in female subjects; and 10.3 (9.5–11.2), 6.8 (6.3–7.4), and 7.3 (6.2–8.6) in both sexes, respectively. No significant seasonal variations were found in incidence of type 1 diabetes in the age-groups 0–14 (P = 0.49), 15–29 (P = 0.53), and 30–49 (P = 0.80) years.

We then assessed the independent roles of age, sex, BMI, and fasting C-peptide on positivity for markers of β-cell autoimmunity (Table 3). Subjects aged 30–39 years had a twofold higher risk of autoimmune diabetes than those aged 40–49 years, and this effect was reduced only slightly in multivariate analysis. Fasting C-peptide values <0.60 nmol/l and BMI <26 kg/m^2 were associated with the highest ORs; these variables were highly correlated (P < 0.0001), and their effects decreased in the multivariate analysis. Individuals with normal weight with fasting C-peptide values <0.60 nmol/l had a more than sixfold higher risk for autoimmune diabetes than individuals with BMI ≥26 mg/kg^2 and C-peptide values ≥0.60 nmol/l, independently of age and sex. No interaction was found between BMI and C-peptide values. Lag of time between date of diagnosis and date of examination for markers of β-cell autoimmunity have been included in logistic regression analysis, obtaining similar results: OR 1.74 (95% CI 0.97–3.16) in female subjects, 2.16 (1.21–3.86) in subjects aged 30–49 years, 2.02 (1.08–3.75) in subjects with BMI <26 kg/m^2, and 3.15 (1.69–5.86) in subjects with fasting C-peptide <0.60 nmol/l. Analysis was also performed us-

Table 3—*Logistic regression analyses of variables associated with ICA or GADA positivity (autoimmune diabetes) or type 1 diabetes in the population-based cohort of incident cases of diabetes in the province of Turin, Italy, aged 30–49 years in the period 1999–2001*

	ICA/GADA positivities		Type 1 diabetes	
	Univariate ORs (95% CI)	Multivariate ORs (95% CI)	Univariate ORs (95% CI)	Multivariate ORs (95% CI)
Sex				
Male	1.00	1.00	1.00	1.00
Female	1.71 (1.07–2.74)	1.60 (0.94–2.75)	1.24 (0.86–1.78)	1.54 (0.92–2.60)
Age (years)				
30–39	2.82 (1.81–4.38)	2.39 (1.40–4.07)	2.99 (2.08–4.28)	2.55 (1.52–4.25)
40–49	1.00	1.00	1.00	1.00
BMI (kg/m^2)				
<26	4.08 (2.55–6.55)	2.17 (1.22–3.85)	4.08 (2.76–6.02)	2.27 (1.32–3.92)
≥26	1.00	1.00	1.00	1.00
Fasting C-peptide				
<0.60 nmol/l	5.21 (3.17–8.55)	3.09 (1.74–5.50)	5.90 (3.67–9.47)	3.63 (2.10–6.29)
≥0.60 nmol/l	1.00	1.00	1.00	1.00

ing type 1 diabetes as dependent variable, obtaining similar ORs (Table 3).

CONCLUSIONS — This study provides the first epidemiological data on the incidence of diabetes in adults in Italy and is one of only a few studies (2,4–7) providing such data for Europe. Although the incidence rate of type 1 diabetes in adults has been considered low, our data show that in Italy, the incidence in the age-group 30–49 years is at least as high as that in the age-group 15–19 years. Large geographical differences in childhood-onset diabetes have been found worldwide, with the highest risk in northern European countries (36 per 100,000 person-years in Finland and 27 per 100,000 person-years in Sweden) and medium risk in Mediterranean countries such as Italy (8.4 per 100,000 person-years) (18,19). Our data are consistent with the hypothesis that these differences could be due, at least in part, to a persistently high risk for adults living in areas at medium or low risk of childhood-onset diabetes. Few data, however, are available for comparison; the only population-based study comparable with ours reported a twofold lower rate in the age-group 40–75 years than in the age-group 0–14 years (10 per 100,000 vs. 27 per 100,000 person-years) in Sweden (4,18). The respective figures in the province of Turin are 10.2 at age 0–14 years and 7.3 at age 30–49 years. In a very-low-risk area for childhood diabetes as China, however, autoimmune diabetes has been found to be rare even in adults (20). Further studies are needed in areas covered by registries to confirm our hypothesis. With respect to 10 years ago, it is clearly established that type 1 diabetes spans all age-groups. Moreover, as recently reviewed (21), the determinants of the disease could be age related; therefore, standardized epidemiological studies that include adults should allow geographical and temporal comparisons of childhood- and adult-onset type 1 diabetes (6), potentially increasing knowledge about the etiology of the disease.

Adult-onset type 1 diabetes is characterized by better-preserved residual β-cell function (13). Because of this, clinical presentation of the disease is often misclassified as type 2 diabetes, making it difficult to depict its epidemiological features (8). Most of the available data have been obtained from registries of subjects with acute-onset type 1 diabetes (1–3,5–7) or of insulin-treated subjects identified through prescription databases (22). Only the studies conducted in Sweden (4,23) have described the incidence of type 1 diabetes defined according to an etiological classification, relying on positivity for markers of autoimmunity rather than on clinical presentation at disease onset. A previous study by our group limited recruitment to subjects with normal weight and found that a high proportion (50%) of subjects aged 30–54 years were defined as having type 1 diabetes (11). The present study extends previous observation to a population-based incident cohort. Validity is assured by the high estimated completeness of ascertainment of both children and young adults, the large proportion (54%) of subjects with autoimmune markers measured in a centralized laboratory, and prospective assessment of clinical features in untested subjects over a 3- to 5-year follow-up period.

According to the classification of diabetes, we considered all subjects undergoing permanent insulin treatment or positivity for ICA or GADA as having type 1 diabetes, irrespective of insulin treatment (9). Of >1,000 incident cases, only 13% were defined as having type 1 diabetes. Of 617 tested subjects, only 15.9% were positive for ICA or GADA. Although markers of β-cell autoimmunity could not be assessed for the whole cohort of incident cases, prospective evaluation of untested subjects during 3–5 years of follow-up increased our confidence that all insulin-dependent subjects had been identified. The subjects tested for autoimmune markers were younger and had lower BMI values and were thus selected for a higher likelihood of having latent autoimmune diabetes than untested subjects. Even if we apply the frequency of positivity for ICA or GADA of tested subjects to all untested subjects, a conservative estimate would be that no more than 16% of subjects aged 30–49 years in our registry had type 1 diabetes, and this would slightly increase our estimated incidence of type 1 diabetes in adults. The proportion with type 1 diabetes with respect to all new cases of diabetes is, however, age related, being 30% in the age-group 30–34 years and only 8% in the age-group 45–49 years. Type of diabetes was correctly classified by diabetologists in 95% of the cohort using clinical criteria only; indeed, in only 51 of 1,135 individuals did the assessment of markers of β-cell autoimmunity allow us to define subjects misclassified as having type 2 diabetes as having type 1 diabetes. Sex differences in the incidence of type 1 diabetes after puberty, with a higher risk for male than female subjects, have been previously reported (13,24–26). Our findings, like others (1,4), provide evidence that this pattern of risk persists up to the age of 49 years for both type 1 and type 2 diabetes, and male subjects have a twofold higher risk than female subjects in all age-groups. This nonspecific pattern of risk would suggest sex-linked differences in β-cell function or in insulin sensitivity, with a higher rate of progression to β-cell exhaustation in male than in female subjects rather than sex differences in the autoimmune pathogenesis of the disease. Our study confirms that younger age and normal weight are predictors of autoimmune diabetes. From a practical point of view, individuals with normal weight and fasting C-peptide values in the lowest quartile (<0.60 nmol/l) have a sixfold higher risk for type 1 diabetes than overweight individuals with C-peptide values >0.60 nmol/l, independently of age and sex. This finding is consistent with previous studies in middle-aged individuals (27) and in those aged >55 years at diagnosis (28).

We found that the incidence of known type 2 diabetes was 50.7 per 100,000 person-years in the age-group 30–49 years, representing the great majority of new cases of diabetes. The risk increases markedly with age, being sevenfold higher in the age-group 45–49 years than in the age-group 30–34 years, irrespective of sex. This finding is consistent with an incidence study conducted in the period 1960–1969 in Rochester, Minnesota, in spite of different criteria employed to define the disease (1). Another Italian population-based study, the Bruneck Study, which prospectively followed up a nondiabetic cohort of almost 1,000 subjects, found a higher rate (760 per 100,000 person-years) at age 40–79 years than those in our study, which, however, included younger subjects (29). Moreover, our data are based on known cases of diabetes only, thus underestimating the incidence of type 2 diabetes. Overweight and obesity were quite common in this cohort (28 and 41%) and increased with age, particularly in female subjects. Mortality risk in Italian diabetic subjects is only 35–40% higher than in the general population (30–31), but risk is markedly higher in the younger age-groups. Our data, therefore, emphasize the need of primary prevention programs to reduce

risk of diabetes and cardiovascular risk in our adult population.

This population-based study therefore shows that *1*) the risk of adults for type 1 diabetes, defined as persistent insulin treatment or positive markers of β-cell autoimmunity, is similar to that found in the same area for people of postpubertal age; *2*) the risks for both type 1 and type 2 diabetes are twofold higher in male than in female subjects in every age-group; *3*) subjects with normal weight with fasting C-peptide levels <0.60 nmol/l have a sixfold higher likelihood of being positive for ICA or GADA than all other subjects; and *4*) the incidence of type 2 diabetes was 50.7 per 100,000 person-years and sevenfold higher in the age-group 45–49 years than in the age-group 30–34 years. Further studies are required to allow geographical comparisons of risks of both childhood and adulthood autoimmune diabetes, the latter being probably higher than previously believed.

APPENDIX

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